REMARKS

I. The amendment raises no new issues.

The amendments to claims 10 and 50 correct obvious typographical errors and raise no new issues or new matter.

II. The rejection under 35 U.S.C. § 103 should be withdrawn.

The Examiner rejected claims 10-13, 41 and 45-50 under 35 U.S.C. § 103, alleging that the subject matter was obvious in view of WO 98/33485 ("Achen II"), in combination with Kurebayashi et al., Jpn. J. Cancer Res 90: 977-81 (1999) ("Kurebayashi"). Applicants request reconsideration of the rejection in view of the following remarks.

As explained in Applicants' submission dated July28, the present application teaches that increased amounts of ***unprocessed*** (i.e., full-length) VEGF-D expressed in tumors correlates with faster tumor growth and increased metastatic risk compared to expression other forms of VEGF-D in tumors (i.e., fully processed or truncated portions of VEGF-D). See, Examples 9 and 13 of the present application.

Achen II generically discloses methods of detecting VEGF-D in a sample and methods of screening for cancer associated with VEGF-D, but Achen II does not specifically disclose or suggest measuring both the amount of unprocessed VEGF-D having a molecular weight of ~ 53K in the sample for ***diagnosing the growth characteristics*** of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample. In fact, Achen II at page 20, line 10 states "**Quantitation** of VEGF-D in cancer biopsy specimens will be useful as an indicator of future metastatic risk" (emphasis added). Thus, Achen II teaches the amount of VEGF-D in the sample, and not a particular form of the VEGF-D (i.e., unprocessed VEGF-D having a molecular weight of ~ 53K), is useful as an indicator of metastatic risk.

Moreover, Achen II also does not specifically disclose that tumors expressing ***unprocessed*** VEGF-D generate more blood and lymphatic vessels than tumors expressing other forms of VEGF-D. The present application is the first disclosure of the association between the amount of ***unprocessed*** VEGF-D and the intensity of the resulting tumors.

In the final Office action, Applicants argument were not refuted, and the Examiner's allegations of "inherency" (from the previous action) were withdrawn, along with the rejection alleging anticipation. In fact, the Examiner acknowledged (at page 3) that Applicants analysis of Achen II was correct:

> The invention differs from the teachings of the reference only in that measuring amount of unprocessed VEGF-D polypeptide having a molecular weight of approximately 53 K in the sample and wherein the increased unprocessed VEGF-D having a molecular weight of approximately 53K in said sample correlates with increased tumor growth or metastatic risk.

In an apparent effort to remedy the deficiencies in the teachings in Achen II, the Examiner cited Kurebayashi. However, the Examiner did not explain – or even allege – how Kurebayashi addresses the shortcomings of Achen II. There is no discussion by the Examiner and no suggestion in the cited reference for ***diagnosing the growth characteristics*** of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample.

In fact, in the discussion of detecting, the Examiner returns to discussing the "4A5" antibody of the Achen II reference. As explained previously, and never refuted by the Examiner, Achen II teaches that the 4A5 antibody was *generated against a processed form* of VEGF-D known as VEGF-DΔNΔC. (See Achen II at pp. 31-32.) Because antibody 4A5 binds to processed VEGF-D (i.e., VEGF-D having a molecular weight of ~21K), a measurement of VEGF-D with the antibody cannot be interpreted as a measurement of the quantity of unprocessed VEGF-D (i.e., VEGF-D having a molecular weight of ~53K). Analysis of a tissue section with an antibody that binds an epitope found in both unprocessed, partly processed, and mature VEGF-D can provide information about the distribution of VEGF-D in the sample and the total quantity of VEGF-D, but does not indicate which forms of VEGF-D are being measured.

Because Achen II (alone or in combination with Kurebayashi) does not specifically disclose methods of screening for a neoplastic disease characterized by an increase in the amount of ***unprocessed*** VEGF-D having a molecular weight of ~53K in cancers, it does not render obvious any of claims 10-13, 41 and 45-50. The rejection should therefore be withdrawn.

III. The finality of the action was premature.

The Examiner alleges, without any explanation, that Applicant's amendments necessitated the new rejection, and on this basis has made the action "final." The Applicants disagree.

Even before issuance of the previous, non-final action, the Applicant's claims were clearly directed to the same subject matter to which they are currently directed. For example, claim 45 included a step pertaining to analysis of the size of the VEGF-D, and language correlating the amount of *unprocessed* VEGF-D to metastatic risk:

> 45. (version from February 28, 2008) A method of diagnosing growth characteristics of a neoplastic disease in an organism, the method comprising:
> (a) obtaining a sample from an organism with a neoplastic disease;
> (b) **measuring amount and size** of VEGF-D polypeptide in said sample; and
> (c) **diagnosing** growth characteristics of the neoplastic disease **from the amount and size** of the VEGF-D measured in step (b), **wherein increased unprocessed VEGF-D** in said sample **correlates with increased tumor growth or metastatic risk**.

It is clear that Applicants have maintained claims consistently directed to the same subject matter and have also maintained a consistent patentability argument. Any decision to switch the basis of rejection from §102 to §103, and from a single reference to multiple references, was not necessitated by Applicant's amendments. The new rejection, though improper, could have been made in a previous action in relation to a previous version of the claims.

IV. Conclusion

For the foregoing reasons, Applicants request withdrawal of all outstanding rejections and allowance of the pending claims. No other fees are believed to be due with the

filing of this paper. However, the Director is authorized to charge any additional fees deemed necessary to Deposit Account No. 13-2855, under order number 28967/5680D.

If the Examiner believes that a telephone conversation would expedite allowance of the claims, she is invited to contact the undersigned attorney for applicants, at the number below.

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Respectfully submitted,

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